REMARKS

Claims 27-49 were pending in the application. Claims 28, 30, 38, 40, 47, and 49 have been cancelled, without prejudice, as being directed to a non-elected invention. Claims 31, 41 and 42 have also been cancelled and claims 32, 35, 36, 42-46 and 48 have been amended. Accordingly, after the amendments presented herein have been entered, claims 27, 29, 32-37, 39, 43-46, and 48 will remain pending.

Support for the amended claims can be found throughout the specification and claims as originally filed. Specifically, support for claims 46, and 48 can be found at, for example, page 3, lines 19-22 of the specification. The amendments to the remainder of the claims were made to correct dependencies due to the cancellation of some of the independent claims.

No new matter has been added. Any cancellation of the claims should in no way be construed as an acquiescence to any of the Examiner's rejections and was done solely to expedite the prosecution of the application. Applicant reserves the right to pursue the claims as originally filed in this or a separate application(s).

Rejection of Claims 31-36, 41-46 and 48 Under 35 U.S. C. § 112, First Paragraph

The Examiner has rejected claims 31-36, 41-46 and 48 under 35 U.S.C. § 112, first paragraph because, according to the Examiner, "the specification, ***while being enabling for the practice of a method of identifying a ligand which binds to a receptor protein comprising the amino acid sequence presented in SEQ ID NO:5 of the instant specification***, does not reasonably provide enablement for the practice of a binding assay which employs anything less than the entire amino acid sequence presented in SEQ ID NO:5 for those reasons of record." (*Emphasis added*).

Applicant traverses this rejection for the reasons of record. However, in the interest of expediting prosecution, and in no way acquiescing to the Examiner's rejection, Applicant has cancelled claims 31 and 41 which are directed to methods employing fragments of SEQ ID NO:2, thereby rendering this rejection moot as it pertains to these claims. Accordingly, Applicant respectfully requests that the Examiner reconsider and withdraw this rejection as it pertains to claims 31 and 41 and the claims that depend thereon.

With respect to claims 46 and 48, and claims depending therefrom, which are directed to methods of identifying compounds that modulate polypeptides that are at least 95% identical to the hVR-

2 molecules and are capable of modulating membrane excitability in a cell, Applicant, again, points the Examiner's attention to Example 14 of the *Revised Interim Written Description Guidelines Training Materials*. Example 14 provides that a claim directed to variants of a protein having SEQ ID NO:3 "that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A→B" with an accompanying specification that discloses a single species falling within the claimed genus, satisfies the requirements of 35 U.S.C. §112, first paragraph for written description. The rationale behind the foregoing conclusion, as presented by the *Written Description Guidelines*, is that "[t]he single species disclosed is representative of the genus because all members have at least 95% structural identity with the reference compound and because of the presence of an assay which Applicant provided for identifying all of the at least 95% identical variants of SEQ ID NO:3 which are capable of the specified catalytic activity." The Guidelines also provide that "***[t]he procedures for making variants of SEQ ID NO:3 are conventional in the art and an assay is described which will identify other proteins having the claimed catalytic activity. Moreover, procedures for making variants of SEQ ID NO:3 which have 95% identity to SEQ ID NO:3 and retain its activity are conventional in the art.***"

Similarly, in the present case, the claims are directed to methods which use isolated nucleic acid molecules encoding hVR-2 polypeptides comprising an amino acid sequence that is at least 95% identical to the amino acid sequence shown in SEQ ID NO:5, wherein the polypeptide is capable of modulating membrane excitability. Furthermore, Applicant has disclosed in the instant specification assays for identifying all of the at least 95% identical variants of SEQ ID NO:5 which encode polypeptides capable of modulating membrane excitability (see, for example, the patch-clamp methods taught by the Applicant in Example 4). Modulation of membrane excitability is readily testable by one of skill in the art by the methods described in the instant specification and by methods well-known in the relevant art. Accordingly, it would require only routine experimentation on the part of one of skill in the art to mutate the VR-2 molecules of the invention and test them for the ability to modulate membrane excitability as described in the specification.

Applicant agrees with the Examiner's indication that Example 14 of the *Revised Interim Written Description Guidelines Training Materials* is mainly directed toward the criteria necessary to satisfy the written description requirement of 35 U.S.C. § 112. However, this example also provides that, "***[t]he procedures for making variants of SEQ ID NO:3 are conventional in the art and an assay is described which will identify other proteins having the claimed catalytic activity. Moreover, procedures for making variants of SEQ ID NO:3 which have 95% identity to SEQ ID NO:3 and retain***

its activity are conventional in the art." Therefore, as indicated by the United States Patent and Trademark Office Guidelines, procedures for making variants that are 95% identical to a given sequence and retain their activity are routine in the art.

Based on the foregoing, Applicant respectfully submits that the skilled artisan would be able to make and use the claimed invention using only routine experimentation. Accordingly, Applicant respectfully requests that the Examiner reconsider and withdraw the foregoing rejection as it relates to claims 46 and 48 and claims depending therefrom.

Rejection of Claim 42 Under 35 U.S. C. § 112, First Paragraph

The Examiner has maintained the rejection of claim 42 under 35 U.S.C. § 112, first paragraph for the reasons of record.

Applicant traverses the forgoing rejection for the reasons of record. However, in the interest of expediting prosecution, and in no way acquiescing to the Examiner's rejection, Applicant has cancelled claim 42, thereby rendering this rejection moot. Accordingly, Applicant respectfully requests that the Examiner reconsider and withdraw the foregoing rejection.

Rejection of Claims 27, 29, 31, 37, 39, 41, and 46 Under 35 U.S.C. § 102 (e)

The Examiner has rejected claims 27, 29, 31, 37, 39, 41, and 46, under 35 U.S.C. § 102(e) as being anticipated by Julius *et al.* (United States Patent No. 6,335,180 B1). In particular, the Examiner is of the opinion that "[t]he amino acid sequence presented in SEQ ID NO:5 of the instant application is identical to the amino acid sequence presented in SEQ ID NO:36 of the Julius *et al.* patent." The Examiner further states that

> [t]he declaration filed on 30 September 2002 under 37 CFR 1.131 has been considered but is ineffective to overcome the Julius et al. reference. Under 37 CFR 1.131 proof of a utility must be shown if the reference discloses a utility. In re Wilkinson, 304 F.2d 637, 134 USPQ 171 (CCPA 1962); In re Moore, 444 F.2d 572, 170 USPQ 260 (CCPA 1971). Julius et al. (starting at line 30 of column 26) disclosed the utility of the protein described therein in an assay to detect capsaicin

and related compounds in a sample, for example. Applicants declaration does not show that the Applicant had contemplated a specific utility for the proteins described therein before the filing of the Julius et al. application.

Applicant traverses this rejection for the following reasons. The *In re Wilkinson* case that the Examiner relies upon provides that, "[s]ince appellants have satisfactorily shown they did everything done by Stephens [the 102 reference used by the examiner for the rejection] prior to the latter's publication date, they have overcome Stephens as a valid ground of rejection." Similarly, in the present case all Applicant needs to show is that he did everything done by Julius *et al.* prior to the latter's publication date. Julius *et al.* cloned the VR-2 polypeptide of SEQ ID NO:36 and showed that this polypeptide is homologous to the rat VR-1 polypeptide (see Example 15 at columns 49-50). Contrary to the Examiner's assertions, Julius *et al.* do not disclose that the VR-2 polypeptide has utility in an assay to detect capsaicin and related compounds in a sample. The section of the Julius *et al.* patent referred to by the Examiner, namely column 26, line 30, pertains to a "capsaicin receptor" and not the VR-2 polypeptide of SEQ ID NO:36. According to the Julius *et al.* specification (see column 6, lines 15-22), a capsaicin receptor is a "i) polypeptide having an amino acid sequence of a native capsaicin receptor polypeptide, ii) a biologically active fragment of a capsaicin receptor polypeptide, iii) biologically active polypeptide analogs of a capsaicin receptor polypeptide, or iv) a biologically active variant of a capsaicin receptor polypeptide." VR-2 is defined as a "capsaicin receptor-related polypeptide or a vanilloid-like receptor (VLR) polypeptide" and ***not*** as a capsaicin receptor (see column 6, lines 32-41). The only uses that are taught by Julius *et al.* for capsaicin receptor-related polypeptides, like VR-2, are general uses, such as uses in screening assays (see column 22, lines 36-42) and uses in diagnostic assays (see column 27, lines 27-32 and column 32, lines 1-12).

As evidenced by the declaration under 37 CFR §1.131, a copy of which is submitted herewith (the original was filed together with Applicant's Amendment and Response to Final Office Action on April 11, 2003), Applicant had cloned the human VR-2 receptor, had determined that this polypeptide is homologous to the rat VR-1 polypeptide, and had contemplated using this receptor in screening assays and diagnostic assays prior to the effective 102(e) date of Julius *et al.*, *i.e.*, ***prior to January 22, 1999***.

Accordingly, Applicant respectfully submits that the invention disclosed in the present patent application was reduced to practice with a contemplated utility by the inventor prior to the effective

date of the Julius *et al.* reference. As such, the Julius *et al.* reference is not available as prior art against the present invention under 35 U.S.C. 102§(e), and Applicant respectfully requests that the Examiner reconsider and withdraw this rejection.

Rejection of Claim 35 under 35 U.S.C. § 103 (a)

The Examiner has rejected claim 35 under 35 U.S.C. § 103(a) as being unpatentable over Julius *et al.* Specifically, the Examiner is of the opinion that

> [b]ecause the Julius *et al.* patent disclosed the fact that the receptor described therein was naturally expressed in neuronal tissue an artisan would have found it *prima facie* obvious to have expressed that protein recombinantly in a neuronal cell line to obtain a more authentic response by that receptor to a test compound.

Applicant respectfully submits that, in view of the declaration under 37 CFR §1.131 submitted herewith, the Julius *et al.* patent is not available as prior art against the instant application. Accordingly the aforementioned rejection is rendered moot and Applicant respectfully requests that the Examiner reconsider and withdraw this rejection.

Rejection of Claim 42 under 35 U.S.C. § 103 (a)

The Examiner has rejected claim 42 under 35 U.S.C. § 103(a) as being unpatentable over Julius *et al.* in view of Chien *et al.*

Applicant respectfully submits that, in view of the cancellation of claim 42, this rejection is rendered moot. Accordingly, Applicant respectfully requests that the Examiner reconsider and withdraw this rejection.

SUMMARY

In view of the foregoing remarks, reconsideration of the rejections and allowance of all pending claims is respectfully requested.

If a telephone conversation with Applicant's attorney would expedite the prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 679-7336.

Respectfully submitted,

12 May, 2003

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